Claims

1. A method of selectively activating and/or targeting stem cells which enables the cells to then be manipulated mechanically in a remote manner.

2. A method according to claim 1 characterised in that the remote manner is a non-contacting manner and in the case of in vivo activating/targeting specifically from outside the body.

3. A method according to claim 1 characterised in that the method comprises magnetically manipulating a stem cell in vivo or in vitro by the association of a magnetisable particle with a stem cell.

4. A method according to claim 1 characterised in that the method comprises

(i) targeting stem cells to the site of repair and/or holding the cells at that site; and

(ii) conditioning and/or differentiating *in vitro* and/or *in vivo*.

5. A method according to claim 1 characterised in that the method comprises the targeting of stem cells *in vivo*.

6. A method according to claim 1 characterised in that the method comprises the manipulation of human stem cells.

7. A method according to claim 1 characterised in that the method comprises tagging the stem cells with magnetisable nanoparticles which can be delivered to or held at, a particular repair site by external magnetic manipulation.

8. A method according to claim 1 characterised in that the method comprises remote activation of specific stem cell membrane receptors.

9. A method according to claim 1 characterised in that the method comprises deposition of stem cells at a site, retaining the cells at the site and remotely activating the cells *in situ* within a patient.

10. A method according to claim 1 characterised in that the method comprises targeting specific receptors on stem cells for remote activation of transmembrane ion channels in stem cells.

11. A method according to claim 1 characterised in that the method comprises early stage differentiation of cell types.

12. A method according to claim 1 characterised in that the method comprises targeting a variety of stem cell receptor types present in human bone marrow stem cells.

13. A method according to claim 12 characterised in that the stem cell receptor types are selected from mechano-activated ion channels e.g. K+ channels (TREK), calcium channels, integrins and surface membrane binding sites, such as RGD.

14. A method according to claim 13 characterised in that the method comprises targeting receptors for external growth factors (e.g. TGFB and BMP2) which have been shown to activate downstream transcription factors such as Runx2 and Osterix, (critical for stem cell differentiation).

15. A method according to claim 1 characterised in that the stem cells are mesenchymal stem cells.

16. A method according to claim 15 characterised in that the method comprises engraftment of human mesenchymal stem cells at the site of injury or repair.

17. A method according to claim 1 characterised in that the method provides therapeutic treatment.

18. A method according to claim 17 characterised in that the therapeutic treatment is selected from gene therapy and tissue engineering.

19. A method according to claim 18 characterised in that the site is a tissue repair site.

20. A method according to claim 1 characterised in that at the functional level the stem cell differentiated as a neuronal cell.

21. A method according to claim 1 characterised in that the method comprises stem cell binding, delivery and activation.

22. A method according to claim 1 characterised in that the method comprises using adult primary marrow human stem cells and/or human embryonic stem cells.

23. A method according to claim 1 characterised in that a bioreactor enables forces to be applied to magnetic particles attached to stem cells cultured in vitro within a multi-well 2D system or in vivo a 3D scaffold-based system.

24. A method according to claim 23 characterised in that the mesenchymal stem cells comprise populations selected from osteogenic, chondrogenic and adipogenic populations.

25. A method according to claim 1 characterised in that the method comprises magnetic activated cell sorting (MACS) with a monoclonal antibody.

26. A method according to claim 25 characterised in that the monoclonal antibody is STRO-1.

27. A method according to claim 23 characterised in that the method includes BMSc culture in monolayer, using 3D scaffolds composed of biodegradable polymers.

28. A method according to claim 27 characterised in that the biodegradable polymer is selected from polylactic acid (PLLA) and a collagen gel.

29. A method according to claim 1 characterised in that the method comprises *ex vivo* manipulation of an *in vivo* process.

30. A method according to claim 1 characterised in that the method comprises the activation and/or targeting of a magnetisable particle with a stem cell.

31. A method of magnetically manipulating a stem cell which comprises the association of a magnetisable particle with a cell characterised in that the method comprises agonising or antagonising ion channels within a cell by the association of a magnetisable particle with a cell.

32. A method according to claims 1 or 31 characterised in that the method includes a differentiation step.

33. A method according to claims 1 or 31 characterised in that the magnetisable particle is associated directly with the stem cell.

34. A method according to claims 1 or 31 characterised in that the method comprises associating the magnetisable particle with an antibody or an enzyme which antibody or enzyme is subsequently associated with the stem cell.

35. A method according to claims 1 or 31 characterised in that the method comprises the introduction of a particle into a stem cell or the attachment of a particle to a stem cell.

36. A method according to claim 35 characterised in that particles are associated intracellularly or extracellularly.

37. A method according to claim 36 characterised in that particles are associated intracellularly.

38. A method according to claim 37 characterised in that the intracellular association comprises association with an internal binding site.

39. A method according to claims 1 or 31 characterised in that the method comprises manipulating a mechanosensitive ion channel in a stem cell characterised in that the method comprises the association of a magnetisable particle with an ion channel, either directly or indirectly.

40. A method according to claim 39 characterised in that particles are associated with the N-terminal region of the ion channel.

41. A method according to claim 39 characterised in that particles are associated with the COOH terminal region of the ion channel.

42. A method according to claim 39 characterised in that the method comprises the remote manipulation of stem cells and/or of agonising or autagonising an ion channel remotely.

43. A method according to claims 1 or 31 characterised in that the method comprises the utilisation of stem cells known to respond to shear stress, cell swelling and membrane stretch and/or external agents.

44. A method according to claim 43 characterised in that the external agent is a fatty acid or a general anaesthetic.

45. A method according to claims 1 or 31 characterised in that the method is incorporated in an application of pain relief, anaesthesia, therapeutics, tissue engineering and repair and/or cancer therapy.

46. A method according to claim 45 characterised in that the stem cell is differentiated to connective or neuronal tissue.

47. A method according to claim 45 characterised in that the stem cell is differentiated to bone, neurons, cardiac cells or any combination thereof.

48. A method according to claim 39 characterised in that the ion channel is a mechanosensitive ion channel.

49. A method according to claim 39 characterised in that the mechanosensitive ion channel has been transfected into a cell.

50. A method according to claim 39 characterised in that the method comprises the use of force resulting in membrane deformation, triggering the opening of the channel or Voltage-gated and ligand-gated ion channels.

51. A method according to claim 50 characterised in that the ion channel is a voltage-gated ion channel.

52. A method according to claim 50 characterised in that the ion channel is a ligand-gated ion channel.

53. A method according to claim 39 characterised in that the ion channel is selected from the group a including sodium channel, potassium channel, calcium channel, chloride channel and a non-selective cation channel or any combination thereof.

54. A method according to claim 53 characterised in that the ion channel is selected from a calcium or a potassium ion channel.

55. A method according to claim 54 characterised in that the ion channel is a potassium ion channel.

56. A method according to claim 55 characterised in that the potassium channel is a TREK-1 channel.

57. A method according to claim 56 characterised in that the method comprises the utilisation of TREK-1 channels in bone cells.

58. A method according to claims 1 or 31 characterised in that the method comprises targeting using an external high gradient rare earth magnet.

59. A method according to claim 58 characterised in that the rare earth magnet is a NdFeB magnet.

60. A method according to claims 1 or 31 characterised in that the magnets produce high field/gradient products which exert a translational force on the magnetic particles loaded onto the cells, holding them at the target site according to the equation:

$$F_{mag} = (X_2 - X_1)V\frac{1}{\mu_o}B(\nabla B)$$

61. A method according to claims 1 or 31 characterised in that the activation comprises remote mechanical activation achieved using a magnetic conditioning bioreactor.

62. A method according to claims 1 or 31 characterised in that the magnetisable particle used in the method of the invention may be inherently magnetic or, alternatively, may be one which reacts in a magnetic field.

63. A method according to claims 1 or 31 characterised in that the magnetisable particle is magnetic.

64. A method according to claim 63 characterised in that the magnetic material is paramagnetic superparamagnetic, ferromagnetic and/or antiferromagnetic,

65. A method according to claim 62 characterised in that the magnetisable material is selected from the group which includes elemental iron (Fe), or a compound thereof, and a chromium compound, or a combination thereof.

66. A method according to claim 65 characterised in that the iron compound is an iron salt.

67. A method according to claim 66 characterised in that the iron salt is selected from the group which includes magnetite (Fe_3O_4), maghemite (γFe_2O_3) and greigite (Fe_3S_4), or any combination thereof.

68. A method according to claim 65 characterised in that the chromium compound is a chromium salt.

69. A method according to claim 68 characterised in that the chromium salt is chromium oxide (CrO_2).

70. A method according to claim 63 characterised in that the magnetic material comprises particles which comprises a magnetic core with a biocompatible coating.

71. A method according to claim 70 characterised in that the biocompatible magnetic nanoparticles comprise a magnetite (Fe_3O_4) and/or maghemite (Fe_2O_3) core with either a silica, dextran, or PVA coating.

72. A method according to claims 1 or 31 characterised in that the particle is a nanoparticle.

73. A method according to claim 72 characterised in that the nanoparticles have a particle size of from 1nm to 10μm.

74. A method according to claim 73 characterised in that the particles have a mean size of 5000 nm or less.

75. A method according to claim 74 characterised in that the particles have a mean size of from 1 nm to 5000 nm.

76. A method according to claim 72 characterised in that the magnetic nanoparticles have a particle size of from 10nm up to a few microns.

77. A method according to claims 1 or 31 characterised in that the coating is functionalized and crosslinked to membrane attachment motifs.

78. A method according to claims 1 or 31 characterised in that the magnetic nanoparticles are modified so as to customise particle internalization frequency, binding efficiency, stability and binding on cell viability and function.

79. A method according to claim 78 characterised in that the modification includes customisation of internal binding sites as well as sites on the outer membrane.

80. A method according to claim 71 characterised in that the particle has a core and a silica shell enveloping the core.

81. A method according to claim 80 characterised in that the particle is selected from those comprising (a) a core comprising a magnetisable particle and (b) a silica shell enveloping the core.

82. A method according to claim 70 characterised in that the particle is a porous particle with multiple magnetic centre within the pores.

83. A method according to claims 1 or 31 characterised in that the method comprises the application of a remote magnetic field on the magnetisable particles.

84. A method according to claim 34 characterised in that the particle is tagged with one or more specific antibodies or protein binding motifs which recognise key cellular elements within a cell.

85. A method according to claim 84 characterised in that the specific antibodies or protein binding motifs are selected from transmembrane extracellular matrix molecules, adhesion molecules or dispersed membrane adhesion proteins or extracellular matrix proteins.

86. A method according to claim 85 characterised in that the transmembrane adhesion molecules are selected from integrins, cadherins, selectins, and immunoglobulins.

87. A method according to claim 86 characterised in that the specific antibodies or protein binding motifs are selected from dispersed membrane adhesion proteins.

88. A method according to claim 87 characterised in that the dispersed membrane adhesion protein is RGD (arginine-glycine-aspartate).

89. A method of treatment of a patient suffering from a disorder in which an ion channel plays a role which comprises the administration to such a patient of magnetisable particles and manipulating stem cell ion channels or the stem cells using a magnetic field external to the body.

90. A method of treatment or alleviation of a tumour cell which comprises a method according to claim 89.

91. A method according to claim 90 characterised in that the tumour cell is a cancer cell.

92. A method of treatment of a patient according to claim 91 characterised in that the method comprises the killing of cells via holding ion channels open with a targeted static magnetic field.

93. A method of treatment of a patient according to claim 91 characterised in that the method comprises the killing of cells via cyclically opening and closing ion channels with a targeted, time-varying magnetic field.

94. A method of treatment according to claim 91 in which a disorder may involve a number of tissues in the body where ion channels play a key role in normal cellular homeostasis.

95. A method according to claim 94 characterised in the cells are cardiac muscle cells.

96. A method according to claim 94 characterised in that the method comprises the treatment of hypertension.

97. A method according to claim 94 characterised in that the method comprises pain relief.

98. A method according to claim 97 characterised in that the method comprises anaesthesia.

99. A method according to claim 98 characterised in that the anaesthesia is localised.

100. A method of treatment of a patient according to claim 89 characterised in that the method comprises tissue and/or bone repair.

101. A method of treatment according to claim 100 characterised in that the cells are selected from ligamentum cells, tenocytes, chondrocytes and other stromal cells (such as chondrocyte progenitor cells).

102. A method of treatment according to claim 100 characterised in that the method comprises the regeneration of tissue or the generation of artificial tissue, such as skin, cartilage, ligament, tendon, muscle or bone.

103. A method of treatment according to claim 100 characterised in that the method comprises the remote activation of ion channels.

104. A method of treatment according to claim 100 characterised in that the method comprises wound healing and/or tissue adhesion.

105. A method of treatment according to claim 100 characterised in that the method comprises bone repair and/or bone growth.

106. A method of treatment according to claim 89 characterised in that the method comprises a dental or veterinary application.

107. A method of treatment according to claim 98 characterised in that the method establishes localised anaesthesia through the action of ion channel modulation by a magnetic field external to the body.

108. A method of treatment according to claim 89 characterised in that the method comprises the use of a magnetic field at a frequency of from 0.1 to 10 Hz.

109. A method of treatment according to claim 89 characterised in that the method comprises the use of a magnetic field will typically have a flux density of from 10 mT to 1400 mT.

110. A method of inducing a therapeutic effect in a stem cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell and magnetically manipulating the magnetisable particle.

111. A method of treatment which comprises the administration of a therapeutically active agent which may be administered simultaneously, separately or sequentially with a magnetisable particle whilst agonising or antagonising ion channels within a stem cell.

112. A method of targeting a therapeutically active agent to a stem cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell, magnetically manipulating the magnetisable

particle and simultaneously, separately or sequentially administering the therapeutically active agent.

113. The use of a magnetisable particle in a method of magnetically manipulating a stem cell wherein the method comprises the association of a magnetisable particle with a cell.

114. The use according to claim 113 characterised in that the use comprises selectively activating and/or targeting stem cells which enables the cells to then be manipulated mechanically in a remote manner.

115. The use according to claim 113 characterised in that the remote manner is a non-contacting manner and in the case of in vivo activating/targeting specifically from outside the body.

116. The use according to claim 113 characterised in that the use comprises magnetically manipulating a stem cell *in vivo* or *in vitro* by the association of a magnetisable particle with a stem cell.

117. The use according to claim 113 characterised in that the use comprises

(i) targeting stem cells to the site of repair and/or holding the cells at that site; and

(ii) conditioning and/or differentiating *in vitro* and/or *in vivo*.

118. The use according to claim 113 characterised in that the use comprises the targeting of stem cells *in vivo*.

119. The use according to claim 113 characterised in that the use comprises the manipulation of human stem cells.

120. The use according to claim 113 characterised in that the use comprises tagging the stem cells with magnetisable nanoparticles which can be delivered to or held at, a particular repair site by external magnetic manipulation.

121. The use according to claim 113 characterised in that the use comprises remote activation of specific stem cell membrane receptors.

122. The use according to claim 113 characterised in that the use comprises deposition of stem cells at a site, retaining the cells at the site and remotely activating the cells *in situ* within a patient.

123. The use according to claim 113 characterised in that the use comprises targeting specific receptors on stem cells for remote activation of transmembrane ion channels in stem cells.

124. The use according to claim 113 characterised in that the use comprises early stage differentiation of cell types.

125. The use according to claim 113 characterised in that the use comprises targeting a variety of stem cell receptor types present in human bone marrow stem cells.

126. The use according to claim 125 characterised in that the stem cell receptor types are selected from mechano-activated ion channels e.g. K+ channels (TREK), calcium channels, integrins and surface membrane binding sites, such as RGD.

127. The use according to claim 126 characterised in that the use comprises targeting receptors for external growth factors (e.g. TGFB and BMP2) which have been shown to activate downstream transcription factors such as Runx2 and Osterix, (critical for stem cell differentiation).

128. The use according to claim 1 characterised in that the stem cells are mesenchymal stem cells.

129. The use according to claim 128 characterised in that the use comprises engraftment of human mesenchymal stem cells at the site of injury or repair.

130. The use according to claim 113 characterised in that the use provides therapeutic treatment.

131. The use according to claim 130 characterised in that the therapeutic treatment is selected from gene therapy and tissue engineering.

132. The use according to claim 131 characterised in that the site is a tissue repair site.

133. The use according to claim 113 characterised in that the at the functional level the stem cell differentiated as a neuronal cell.

134. The use according to claim 113 characterised in that the use comprises stem cell binding, delivery and activation.

135. The use according to claim 113 characterised in that the use comprises using adult primary marrow human stem cells and/or human embryonic stem cells.

136. The use according to claim 113 characterised in that the bioreactor enables forces to be applied to magnetic particles attached to stem cells cultured in vitro within a multi-well 2D system or in vivo a 3D scaffold-based system.

137. The use according to claim 136 characterised in that the mesenchymal stem cells comprise populations selected from osteogenic, chondrogenic and adipogenic populations.

138. The use according to claim 1 characterised in that the use comprises magnetic activated cell sorting (MACS) with a monoclonal antibody.

139. The use according to claim 138 characterised in that the monoclonal antibody is STRO-1.

140. The use according to claim 136 characterised in that the use includes BMSc culture in monolayer, using 3D scaffolds composed of biodegradable polymers.

141. The use according to claim 140 characterised in that the biodegradable polymer is selected from polylactic acid (PLLA) and a collagen gel.

142. The use according to claim 113 characterised in that the use comprises *ex vivo* manipulation of an *in vivo* process.

143. The use according to claim 113 characterised in that the use comprises the activation and/or targeting of a magnetisable particle with a stem cell.

144. The use of a magnetisable particle in the manufacture of a therapy that comprises agonising or antagonising ion channels within a stem cell by the association of the magnetisable particle with a stem cell.

145. The use according to claims 113 or 144 characterised in that the use includes a differentiation step.

146. The use according to claims 113 or 144 characterised in that the magnetisable particle is associated directly with the stem cell.

147. The use according to claims 113 or 144 characterised in that the use comprises associating the magnetisable particle with an antibody or an enzyme which antibody or enzyme is subsequently associated with the stem cell.

148. The use according to claims 113 or 144 characterised in that the use comprises the introduction of a particle into a stem cell or the attachment of a particle to a stem cell.

149. The use according to claim 148 characterised in that particles are associated intracellularly or extracellularly.

150. The use according to claim 149 characterised in that particles are associated intracellularly.

151. The use according to claim 150 characterised in that the intracellular association comprises association with an internal binding site.

152. The use according to claim 113 or 144 characterised in that the use comprises manipulating a mechanosensitive ion channel in a stem cell characterised in that the use comprises the association of a magnetisable particle with an ion channel, either directly or indirectly.

153. The use according to claim 152 characterised in that particles are associated with the N-terminal region of the ion channel.

154. The use according to claim 152 characterised in that particles are associated with the COOH terminal region of the ion channel.

155. The use according to claim 152 characterised in that the use comprises the remote manipulation of stem cells and/or of agonising or autagonising an ion channel remotely.

156. The use according to claim 113 or 144 characterised in that the use comprises the utilisation of stem cells known to respond to shear stress, cell swelling and membrane stretch and/or external agents.

157. The use according to claim 156 characterised in that the external agent is a fatty acid or a general anaesthetic.

158. The use according to claim 113 or 144 characterised in that the use is incorporated in an application of pain relief, anaesthesia, therapeutics, tissue engineering and repair and/or cancer therapy.

159. The use according to claim 158 characterised in that the stem cell is differentiated to connective or neuronal tissue.

160. The use according to claim 158 characterised in that the stem cell is differentiated to bone, neurons, cardiac cells or any combination thereof.

161. The use according to claim 152 characterised in that the ion channel is a mechanosensitive ion channel.

162. The use according to claim 152 characterised in that the mechanosensitive ion channel has been transfected into a cell.

163. The use according to claim 152 characterised in that the use comprises the use of force resulting in membrane deformation, triggering the opening of the channel or Voltage-gated and ligand-gated ion channels.

164. The use according to claims 163 characterised in that the ion channel is a voltage-gated ion channel.

165. The use according to claims 163 characterised in that the ion channel is a ligand-gated ion channel.

166. The use according to claim 152 characterised in that the ion channel is selected from the group a including sodium channel, potassium channel, calcium channel, chloride channel and a non-selective cation channel or any combination thereof.

167. The use according to claim 166 characterised in that the ion channel is selected from a calcium or a potassium ion channel.

168. The use according to claim 167 characterised in that the ion channel is a potassium ion channel.

169. The use according to claim 168 characterised in that the potassium channel is a TREK-1 channel.

170. The use according to claim 169 characterised in that the use comprises the utilisation of TREK-1 channels in bone cells.

171. The use according to claims 113 or 144 characterised in that the use comprises targeting using an external high gradient rare earth magnet.

172. The use according to claim 171 characterised in that the rare earth magnet is a NdFeB magnet.

173. The use according to claims 113 or 144 characterised in that the magnets produce high field/gradient products which exert a translational force on the

magnetic particles loaded onto the cells, holding them at the target site according to the equation:

$$F_{mag} = (X_2 - X_1)V\frac{1}{\mu_o}B(\nabla B)$$

174. The use according to claims 113 or 144 characterised in that the activation comprises remote mechanical activation achieved using a magnetic conditioning bioreactor.

175. The use according to claims 113 or 144 characterised in that the magnetisable particle used in the use of the invention may be inherently magnetic or, alternatively, may be one which reacts in a magnetic field.

176. The use according to claims 113 or 144 characterised in that the magnetisable particle is magnetic.

177. The use according to claim 176 characterised in that the magnetic material is paramagnetic superparamagnetic, ferromagnetic and/or antiferromagnetic,

178. The use according to claim 175 characterised in that the magnetisable material is selected from the group which includes elemental iron (Fe), or a compound thereof, and a chromium compound, or a combination thereof.

179. The use according to claim 178 characterised in that the iron compound is an iron salt.

180. The use according to claim 179 characterised in that the iron salt is selected from the group which includes magnetite (Fe_3O_4), maghemite (γFe_2O_3) and greigite (Fe_3S_4), or any combination thereof.

181. The use according to claim 178 characterised in that the chromium compound is a chromium salt.

182. The use according to claim 181 characterised in that the chromium salt is chromium oxide (CrO_2).

183. The use according to claim 176 characterised in that the magnetic material comprises particles which comprises a magnetic core with a biocompatible coating.

184. The use according to claim 183 characterised in that the biocompatible magnetic nanoparticles comprise a magnetite (Fe_3O_4) and/or maghemite (Fe_2O_3) core with either a silica, dextran, or PVA coating.

185. The use according to claims 113 or 144 characterised in that the particle is a nanoparticle.

186. The use according to claim 185 characterised in that the nanoparticles have a particle size of from 1nm to 10μm.

187. The use according to claim 187 characterised in that the particles have a mean size of 5000 nm or less.

188. The use according to claim 187 characterised in that the particles have a mean size of from 1 nm to 5000 nm.

189. The use according to claim 185 characterised in that the magnetic nanoparticles have a particle size of from 10nm up to a few microns.

190. The use according to claims 113 or 144 characterised in that the coating is functionalized and crosslinked to membrane attachment motifs.

191. The use according to claims 113 or 144 characterised in that the magnetic nanoparticles are modified so as to customise particle internalization frequency, binding efficiency, stability and binding on cell viability and function.

192. The use according to claim 191 characterised in that the modification includes customisation of internal binding sites as well as sites on the outer membrane.

193. The use according to claim 184 characterised in that the particle has a core and a silica shell enveloping the core.

194. The use according to claim 193 characterised in that the particle is selected from those comprising (a) a core comprising a magnetisable particle and (b) a silica shell enveloping the core.

195. The use according to claim 183 characterised in that the particle is a porous particle with multiple magnetic centre within the pores.

196. The use according to claims 113 or 144 characterised in that the use comprises the application of a remote magnetic field on the magnetisable particles.

197. The use according to claim 147 characterised in that the particle is tagged with one or more specific antibodies or protein binding motifs which recognise key cellular elements within a cell.

198. The use according to claim 197 characterised in that the specific antibodies or protein binding motifs are selected from transmembrane extracellular matrix molecules, adhesion molecules or dispersed membrane adhesion proteins or extracellular matrix proteins.

199. The use according to claim 198 characterised in that the transmembrane adhesion molecules are selected from integrins, cadherins, selectins, and immunoglobulins.

200. The use according to claim 199 characterised in that the specific antibodies or protein binding motifs are selected from dispersed membrane adhesion proteins.

201. The use according to claim 200 characterised in that the dispersed membrane adhesion protein is RGD (arginine-glycine-aspartate).

202. The use of a magnetisable particle in association with a stem cell in the manufacture of a therapy for the treatment of a patient suffering from a disorder in which an ion channel plays a role which comprises the administration to such a patient of magnetisable particles and manipulating the stem cell ion channels or the stem cells using a magnetic field external to the body.

203. The use of a magnetisable particle in the manufacture of a system for targeting a therapeutically active agent to a cell which comprises agonising or antagonising ion channels within the cell by the association of a magnetisable particle with the cell, magnetically manipulating the magnetisable particle and simultaneously, separately or sequentially administering the therapeutically active agent.

204. A kit comprising a therapeutically active agent and means for associating a magnetisable particle with a cell.

205. A method or use substantially as described with reference to the accompanying drawings.